

U.S.S.N. 09/704,362
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AMENDMENT

AMENDMENT TO THE CLAIMS:

The listing of claims will replace all prior versions and listings of claims in the application. Claims 23, 42, 44, 46, and 48 are amended; and claims 50-53 are added.

Claims 1-22 previously cancelled.

23. (currently amended) A computer-based method for predicting clinical responses in patients based on genetic polymorphisms, comprising:
identifying proteins that are the products of a gene exhibiting genetic polymorphisms;

~~obtaining one or more amino acid sequences for~~ of the target protein
~~proteins that is the product~~ are the products of a gene exhibiting genetic polymorphisms;

~~generating 3-D protein structural variant models from the~~
~~sequences~~ determining 3-dimensional (3-D) protein structural variant models for
the proteins that are the products of a gene exhibiting genetic polymorphisms;

building a relational database of protein structural variants based on genetic polymorphisms and observed clinical data associated with particular polymorphisms exhibited in the patients, wherein the database comprises:

3-D molecular coordinates for structural variant-drug complex models; and

observed clinical data associated with the genetic polymorphisms;

obtaining a ~~target~~ protein structural variant encoded by a gene exhibiting genetic ~~polymorphism~~ polymorphisms in a patient;

~~generating~~ determining a 3-D protein model based on the patient's gene sequence of a protein exhibiting polymorphisms ~~patient's gene sequence;~~

screening or comparing the 3-D model of the protein ~~derived~~ from the patient to the structures contained in the database by:

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identifying structures in the database that are similar to the model derived from the ~~patient~~ patient's protein; and

predicting a clinical outcome for the patient based on the clinical data associated with the identified structures.

Claims 24-40 (previously cancelled)

41. (previously presented) The method of claim 23, that further includes the steps of providing the database with a molecular graphics interface that interfaces with the database for 3-D molecular structure visualization;

providing the database with functionality that interfaces with the database for protein sequence and structural analysis; and

providing the database with searching tools that interface with the database.

42. (currently amended) The method of claim 23, wherein the step of ~~generating~~determining 3-D protein structural variant models ~~from the sequences~~ is performed by a method selected from the group consisting of experimental methods, searching protein structure databases, homology modeling, molecular modeling, de novo protein folding, computational protein structure prediction, *ab initio* methods and combinations thereof.

43. (previously presented; withdrawn from consideration) The method of claim 42, wherein the experimental methods include x-ray crystallography and NMR spectroscopy.

44. (currently amended) The method of claim 23, wherein the step of ~~generating~~determining 3-D protein structural variant models ~~from the sequences~~ is performed by a combination of homology modeling and *ab initio* methods.

45. (previously presented) The method of claim 23, wherein the database further comprises 3-D molecular structural data of structural variant models.

46. (currently amended) The method of claim 41, wherein the step of ~~generating~~determining 3-D protein structural variant models ~~from the sequences~~ is performed by a method selected from the group consisting of experimental

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methods, searching protein structure databases, homology modeling, molecular modeling, de novo protein folding, computational protein structure prediction, *ab initio* methods and combinations thereof.

47. (previously presented; withdrawn from consideration) The method of claim 46, wherein the experimental methods include x-ray crystallography and NMR spectroscopy.

48. (currently amended) The method of claim 41, wherein the step of ~~generating~~determining 3-D protein structural variant models ~~from the sequences~~ is performed by a combination of homology modeling and *ab initio* methods.

49. (previously presented) The method of claim 41, wherein the database further comprises 3-D molecular structural data of structural variant models.

50. (New) A computer-based method for predicting clinical responses in patients based on genetic polymorphisms, comprising:

determining a 3-D protein model based on a patient's gene sequence of a gene that exhibits polymorphisms;

screening or comparing the 3-D model of the protein from the patient to the 3-D structures contained in a database of 3-D protein structures by:

identifying structures in the database that are similar to the model of the protein derived from the patient; and

predicting a clinical outcome for the patient based on clinical data associated with the identified structures.

51. (New) The method of claim 50, wherein the step of determining a 3-D protein model is performed by a method selected from the group consisting of experimental methods, searching protein structure databases, homology modeling, molecular modeling, de novo protein folding, computational protein structure prediction, *ab initio* methods and combinations thereof.

52. (New) The method of claim 51, wherein the experimental methods include x-ray crystallography and NMR spectroscopy.

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53. (New) The method of claim 50, wherein the step of determining a 3-D protein model is performed by a combination of homology modeling and *ab initio* methods.